LifePoint

February 25, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket Number 2003D-0522

Enclosed, please find our comments to the Draft Guidance for Industry and FDA Staff: Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests.

Thank you for your consideration.

Sincerely,

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2003D-0522 C4

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WRITTEN COMMENTS REGARDING FDA DRAFT GUIDANCE FOR "PREMARKET SUBMISSION AND LABELING RECOMMENDATIONS FOR DRUGS OF ABUSE SCREENING TESTS dated December 2, 2003

February 25, 2004

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LifePoint, Inc. (Ontario, Calif.) has developed and is manufacturing and marketing a unique on-site product that will test for both alcohol and drugs without the use of breath, blood or urine (see **Exhibit**). The LifePoint® IMPACT® Test System uses a special patented flow immunosensor technology, for which the company holds an exclusive worldwide license from the United States Navy Research Laboratories. When used in conjunction with saliva as the test specimen, this unique technology has made it possible for LifePoint to develop a broadly applicable, non-invasive, on-site diagnostic test system that is capable of providing completely automated results for up to 10 analytes in minutes.

When applied to substance of abuse testing, the LifePoint product brings the advantages of observable, non-invasive collection, quantitative results that may prove to be evidential for alcohol, and significantly more sensitive and specific results than that which is provided by current immunological on-site drug tests. The system, completely automated from collection and processing of the specimen, testing, analysis, result readout and interpretation, almost eliminates the chances for operational or interpretive error and potential specimen mix-up, and, therefore, should provide legally defensible results.

All of these benefits can mean significant cost savings and operational improvements for substance of abuse testing in the workplace, insurance and sports, which are usually conducted by trained professionals under the supervision of a Medical Review Officer (MRO). Furthermore, it is apparent that the standards set for the regulated workplace through the Substance Abuse and Mental Health Services Administration (SAMHSA), Department of Health and Human Services (HHS) (similar to the oversight provided by the Department of Transportation (DOT) for alcohol testing) are being widely adopted as the standards by professionals in the non-regulated workplace arena.

Over the past few years, LifePoint has presented its technical findings at numerous conferences and seminars. LifePoint has presented at the Drug and Alcohol Testing Industry Association, the International Chiefs of Police Drug Recognition Expert Conference, the International Congress of Alcohol, Drugs and Traffic Safety, the Mid-Atlantic Association of Forensic Toxicologists, the Northwest Association of Forensic Toxicologists, the International Association of Forensic Toxicologists, the Society of Forensic Toxicologists, and the American College of Emergency Physicians. In fact, audiences of employers, law enforcement officials, government representatives, medical professionals, scientists and researchers have consistently shown a great deal of interest in the flow immunosensor technology. We have already conducted many field evaluations and studies and overall the product shows greater than 90% agreement with GC/MS test results (the "Gold Standard" detection method for this type of analysis).

With such a tremendously positive response to LifePoint's saliva-based, on-site simultaneous test for drugs of abuse and alcohol, we feel it necessary to

comment on the recently published "Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests". While we acknowledge that there may be a need to set guidelines for OTC products in environments where there are casual, infrequent users, such as in home use, the application of these same guidelines to the more routine, *professional use* in the workplace, sports and insurance is *not* appropriate. The unintentional consequences of duplicate and onerous requirements on both the user and the manufacturer by FDA, in conjunction with the current and proposed DOT and SAMHSA guidelines, will have significant, undesired effects on drug testing in general. Not only will there be a significant increase in the total delivery cost of a test, but the proposed guidelines will also be in conflict with the standards of practice already established and controlled by SAMHSA and DOT.

For example, routine breath alcohol testing has been performed in *professional use* testing environments for over 40 years without FDA oversight. The evidential breath alcohol equipment produced by companies such as CMI, Drager, Intoximeters, can be complex, require frequent calibration and QC testing, extensive user training and certification, and yet these products do not require FDA clearance for use in the workplace, sports and insurance markets. The requirement for FDA clearance for much simpler and easier to-use drug screening products is unfair and reflects bias toward laboratory-based drug of abuse testing.

Of greater concern, these proposed guidelines are significantly more stringent than even those needed to obtain Prescription Use Product 510(k) FDA clearance. It is onerous and unnecessarily burdensome to require more extensive testing, data and labeling for these simple and easy-to-use products than is currently required to obtain FDA clearance for complex laboratory tests requiring complex equipment and significant training. This appears to be a significant departure from the least burdensome approach that the FDA says it is purporting to support.

Lastly, although some of the newer products and technologies under development or recently being marketed have already addressed many of the concerns raised by this document, this guidance focuses on older technologies – such as on-site urine tests. It is critical, for FDA to take into consideration the newer technologies and products that are now available and that can revolutionize substance abuse testing practices. These products and technologies not only provide the ability to obtain lab-quality results easily, quickly, and cost-effectively on-site by non-technical users, but often include operator independent methods that can provide "error-proof" results.

Of great concern, because there are available operator-independent products, the complexity of the test itself should also be addressed as is currently done by FDA in laboratory regulation by defining products as CLIA-88 waived, moderate complexity, or high complexity and using appropriate regulation and labeling

based on the complexity of the product itself. It is completely inappropriate and burdensome for FDA to require workplace, insurance, sport and school testing to develop a laboratory-type environment with QC testing, etc, in order to continue their current testing practices. This is especially unfair when many of the service providers that offer these same testing services are not regulated or certified. Any increase in regulation will have a significant negative impact on drug testing – it will simply become more expensive and difficult to obtain. The unintended consequences is that although testing has been shown in many studies to be the most effective deterrent to drug use, the implementation of FDA proposed guidelines will most certainly have the opposite effect, and eliminate much of the testing currently being performed.

The whole issue of user specific data generation and labeling is also very problematic as proposed. First, it is overly burdensome to require clinical data for each subset of professional use market. To require a manufacturer to try to perform difficult and expensive clinical trails in every single sub-market is overly burdensome, onerous and unfair. This is especially true in some markets where the positivity rate is very low; it will take significant numbers of samples to obtain the needed number of positive results. A single clinical trial, using a few representative sites for professional use should be sufficient. Alternatively, two or three consumer acceptance type studies showing similar performance characteristics in the hands of different users should also suffice.

If the manufacturer has already obtained FDA prescription clearance, only studies required for CLIA-waived status should be performed for workplace, insurance, and sports settings. This would model the validation procedures required of clinical assays being conducted outside of a central lab.

Additionally, according to the proposed guidelines, a manufacturer will need to use user-specific labeling in each market. This becomes very problematic to implement when manufacturers, distributors, and even some service providers offer these products and services in multiple markets. It is overly burdensome and onerous to require the manufacture, distributor and users to manufacture, distribute and use a different product for each of these slightly different submarkets of the professional use category. As identified by FDA, these users have similar levels of training and skills and should not require such specific labeling to ensure proper use.

Additionally, FDA regulation of the professional repetitive use markets such as the workplace, insurance and sports will be duplicative and potentially onerous, costly and confusing to the users and manufacturers. Other governmental agencies already regulate these markets. The Department of Transportation regulates alcohol testing for the workplace, insurance, and sports settings. Likewise, FDA should consider that SAMHSA regulates drugs of abuse testing for the workplace, and the IOC and NCAA regulate sports testing. These markets

already have standards of practice that have been used successfully for a long time, and have been supported by state and federal courts and legislatures.

Lastly, and most importantly, FDA's mission, as authorized by law (21 USC § 393) is to "protect the public health by ensuring that... there is reasonable assurance of the safety and effectiveness of devices intended for human use." "The term "device" means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar related article, including any component, part, or accessory, which is ... intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, in man or other animals..." (21 USC § 321h). The inclusion of workplace, sports and insurance testing is not within the charter of FDA. Additionally, the results of these tests are not used for diagnosis or treatment, and this position has been upheld both by the courts and Congress, which has been explicit on this point in the Americans with Disabilities Act of 1990.

We recognize the mammoth effort that the draft represents on the part of FDA. While we appreciate your effort, we also appreciate the opportunity to submit these comments and respectfully petition your full consideration of the following:

ON-SITE TESTING

The development of simple, easy-to-use drug testing products have enhanced substance abuse detection and allow for more reliable, accurate, and faster testing methods without increasing the cost of such testing. Although there is mention of these tests, there is no real attempt to include these newer and improved technologies and alternative specimen types, such as saliva, in the draft guidance in a manner that is technically appropriate to either on-site methods and technologies and/or alternative test samples; the draft guidelines appear to use instrumented, lab-based urine tests as the standard for testing, data, and labeling. Where on-site tests are mentioned, there is a significant negative bias as to the performance of on-site urine tests, which have not been validated by the studies done to-date. These products perform much better than the proposed labeling suggests.

Additionally, the proposed guidelines lean very heavily toward laboratory-type Prescription Use Product oversight and control, which is not relevant to use in on-site testing in non-medical markets. In fact, many of the draft guidelines require more manufacturer performance testing and user quality control of on-site testing than that currently required for moderately complex laboratory products or lab-based testing.

If the intent of these guidelines is to discourage the use of on-site testing, then this draft guideline will surely accomplish such a goal. However, if instead the goal of these guidelines is to improve the overall accuracy, effectiveness, and efficiency of non-laboratory testing, then the use of Prescription Use Product

oriented regulations and oversight requirements for such simple on-site testing products is overkill. We need only look back to the late 1980s to see how such over-regulation can actually harm the public good rather than help it. Prior to the implementation of the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), most physician offices performed a wide variety of tests that enhanced the physician's ability to provide immediate diagnosis to their patients. The patients and physicians both enjoyed the benefits of this process. With the passage of CLIA-88 and the requirement for physician office labs (often using very simple and automated test products designed for physician office use) to meet the same standards as commercial labs (including hiring laboratory professionals) 85% of physician offices that were doing on-site testing for moderately complex tests stopped testing (CDC data).

SALIVA TESTING

Saliva has been validated as a drug test specimen and represents a viable alternative for drug testing programs. The use of saliva rather than urine makes it possible to address a number of burdensome issues that have plagued drug testing for many years. For example, saliva is, by far, a much less invasive specimen for collection purposes. Few people find it offensive to provide a saliva sample versus urine. Saliva also makes it possible to conduct an observed collection *every time* without requiring anyone to watch a donor urinate.

Because of saliva's window of detection of several hours to a day, depending on the drug and dosage level, it makes for an excellent indicator of "under the influence" status. This makes it particularly effective as a more accurate post-accident, reasonable suspicion test, and even fit-for-duty testing. Additionally, all urine and saliva-based drug tests are "recent use" tests and as such have the capability to be used for pre-employment, random, and return-to-duty testing; in fact, with some drugs, depending on dose level and assay sensitivity, the window of detection for saliva will definitely overlap that of urine. SAMHSA has validated the use of saliva for substance abuse testing for most types of drug tests. Saliva has already been validated and approved in many states as a viable specimen for use in the criminal justice system. Law enforcement officials are specifically allowed by law to use saliva as a specimen for DUI drug testing purposes in many states either by specific reference or under the use of "other bodily substances" besides breath, urine and blood. Lastly, several participants in the European Union-funded ROSITA project have published the results of their studies and have defined the "perfect on-site drug test" as a saliva-based instrument (for objectivity and elimination of user interpretation) panel test, with results in 5 minutes.

Interest in the use of saliva for drug testing purposes is growing rapidly and the guideline should not only reflect this, but also be careful not to inadvertently restrict or discourage its use. This is especially true at a time when adulteration and substitution problems associated with urine testing are beginning to impact

the integrity of the drug testing process overall, and the use of a specimen that can be observed every time significantly reduces the opportunity for substitution and adulteration.

Unfortunately, these guidelines do not take into consideration the different issues and requirements needed when using saliva as a test specimen. For example, drug levels in saliva are much lower than in urine. Because of this, the technological challenges for saliva testing are much greater. The use of the same requirements for precision and accuracy for the much lower levels of drugs found in saliva is inappropriate; the +/- percentages for determining the precision and accuracy for a 5 ng/ml sample should be significantly different that for 2000 ng/ml sample. Even laboratories have been shown by a SAMHSA study to have significant lab-to-lab variation at these low levels. To require a manufacturer to meet standards that even laboratories have difficulty meeting is unfair and burdensome.

THE DRAFT GUIDELINE POINT-BY-POINT

The following are recommendations that LifePoint believes should be considered by FDA.

INTRODUCTION

The first paragraph statues that this guidance is for premarket notification submissions and labeling for *in vitro* diagnostic (IVD) devices intended to screen for drugs of abuse; however, the testing done in workplaces, schools, and for sports and insurance is not for diagnostic purposes, only forensic purposes. Therefore, the application of these guidelines to the proposed markets is not appropriate, and outside the charter of FDA (see above).

Although the introduction states that the guidance is for screening tests using urine, hair, saliva or other matrices, urine is used throughout the document for reference examples. More importantly, the guidance provided in this document reflects a similarity to 510(k) Prescription Use FDA submission requirements for instrumented, lab-based urine testing products and methods, with no consideration given to the differing requirements of other technologies and sample matrixes.

More importantly, there are significant inconsistencies in these proposed guidelines that conflict with standards that are already applied in certain industries which are already regulated by the US Government: SAMHSA and DOT already regulate drug testing in the workplace (similar to DOT regulation of alcohol testing), and SAMHSA is currently completing a major effort to increase that oversight. We continue to see that testing in the workplace is moving toward professional use in both the regulated and non-regulated workplace. Additionally, oversight is provided to drug testing in sports medicine through the

International Olympic Committee (IOC) and the National College Athletic Association (NCAA).

Additionally, the FDA proposed guidance for professional use products is almost identical to those required for laboratory use products. It is not appropriate to apply the same standards for products used by highly trained laboratory personnel to frequent users, who do not generally have the same level of scientific education and technical training.

Within the professional use settings of workplace, sports and insurance, there may be a need to provide data that shows that inexperienced users can use a specific product with reliable results, similar to the types of studies used for a CLIA waver. But, within that context, it should be adequate to show: 1) a product gives results similar to a predicate device, and 2) a non-trained user will obtain results similar to a trained professional. The test system should provide both the non-trained user and the professional equal ability to obtain valid test results and should not require any correlation to a reference method (this is in the prescription part of the guidelines).

Lastly, there is no consideration given to the complexity of the product being used; for example, it is not clear how CLIA-88 waived type products would be used in a professional or home use environment compared with moderate complexity products. FDA needs to consider how the complexity of the products being used would change the oversight requirements in these environments. Since CLIA waived products assure an accurate result by a non-technical user, many of the proposed regulations are again inconsistent in the application of such products in an OTC environment.

OTC products are mostly used in environments where there are casual and infrequent operators of the product(s), and because of that, these users may require more assistance from the manufacturer of a product.

LifePoint recommends that FDA ultimately consider several different levels of oversight to any testing process, depending on both the user level of familiarity with testing procedures in general, and the complexity of the product being used. For example, there may be the need for several levels of oversight and control such as:

1) OTC Home Use – non-experienced user.
   a) Simple or automated product with no user interpretation (such as CLIA waived products)
   b) Products that are somewhat complex and that require user interpretation
2) Workplace, Sports Medicine and Insurance Testing – Testing done by professionals under the oversight and control of SAMHSA, DOT, the NCAA, and the IOC.

a) Simple or automated products with no user interpretation (such as CLIA waived products)
b) Products that are somewhat complex and that require user interpretation

3) Laboratory Based Testing
   a) CLIA Waived Products
   b) Moderate Complexity Products
   c) High Complexity Products

SAMHSA is already addressing these issues in the workplace and currently has a draft guidance that takes into consideration the complexity of various products and technologies.

The unintentional consequences of duplicate and onerous regulatory requirements on the user and the manufacturer by FDA, in conjunction with the proposed DOT and SAMHSA guidelines, will have significant, undesired effects on drug testing in general by significantly increasing the cost, and decreasing the amount of testing being performed. It has been validated numerous times that testing routinely for drugs is the best deterrent for drug use. We firmly believe, therefore, that melding FDA's guidelines within the framework of the guidelines that already exist, such as those of SAMHSA and DOT, will do more to promote public health and safety than an independent guideline will provide.

II. DEVICE DESCRIPTION

The product codes listed for the various drugs do not include all of the currently available and commonly used methods; for example, not all immunoassays are enzyme immunoassays. Specifically, the following methods/technologies need to be added to the list:

Amphetamine Test System
Immunoassay, Amphetamine

Cocaine and Cocaine Metabolite Test System
Immunoassay, Cocaine
Immunoassay, Cocaine and Cocaine Metabolites

Methamphetamine
Immunoassay, Methamphetamine
Enzyme immunoassay, Methamphetamine

Opiate Test System
Immunoassay, Opiate

Cannabinoid Test System
Immunoassay, Cannabinoids

Phencyclidine Test System
Immunoassay, Phencyclidine

III. PERFORMANCE CHARACTERISTICS

A. OVERVIEW

The development of newer technologies and products has significantly increased the level of accuracy that can be obtained from some on-site test systems. It is inappropriate to classify all on-site methods as "less accurate" than lab-based methods. In fact, some of the newer methods may be as, or more accurate than some lab-based methods.

The requirement to compare a simple screening device to the "gold standard" GC/MS is overly burdensome and onerous. Even highly complex, lab-based tests are not currently required to meet this standard for Prescription Use 510(k) FDA submissions; they are only required to show equivalence to a predicate device. This proposed standard is unreasonable and unfair and shows a bias against these simple on-site products.

The requirement for extensive labeling on false positive and false negative results is also not appropriate. Some drugs (cocaine, PCP or THC) being tested, rarely, if ever, get either laboratory false positives or positives from prescription medications. Therefore, if an on-site test is as accurate as a lab-based test, then a confirmation test should be performed only as desired by the user. We suggest the requirement for language that indicates that: "presumptive positive results for certain drugs (for example opiates and amphetamines) may be caused by prescription or OTC drugs and a confirmation test is strongly suggested".

B. GENERAL STUDY CONSIDERATIONS

Table 1 identifies the proposed requirements for each of the types of studies needed for FDA submissions. With one exception, the proposed requirements for workplace or other professional use products are identical to laboratory use products. It is not appropriate to apply the same standards for products used by highly trained laboratory personnel to frequent users, who do not generally have the same level of scientific education and technical training. With only two exceptions, the proposed requirements for OTC Home Use products are identical to laboratory use products. It is even more inappropriate to apply the same standards for products used by highly trained personnel to consumers that would infrequently use a product.

The study design criteria show the lab-based urine sample bias of the proposed guidelines. For example, it is simple to obtain multiple samples to test numerous times from a single urine sample of greater than 50 ml – the sample is the same

throughout and should give similar results for all tests performed. If however, one is now to apply the same standards to a saliva sample with a direct test done on the sample, the ability to run numerous tests does not exist, since each sample is collected separately, each sample is different. Therefore, it is not possible to test the same sample numerous times. This could provide different results when a sample is very near the cutoff, and, more importantly, for example, makes it impossible to use clinical samples for certain types of data collection or precision testing.

As a note, the guideline specifically calls for a "clinical sample diluted with known negative urine". This should be changed to "clinical sample diluted with known negative sample". However, as a note, this cannot be done with some types of samples such as saliva, sweat and hair testing.

C. SPECIFIC PERFORMANCE STUDIES

1. Cutoff Characterization

The use of threshold cutoff concentrations as identified by SAMHSA is appropriate to a degree; however, we as a manufacturer have identified more appropriate cutoffs for some of our assays based upon our clinical data. It is critical that a manufacturer be allowed to determine their own thresholds based on their own clinical data. Currently, FDA does not require manufacturers of IVD products to conform to a standard and instead relies on the performance of the specific product and manufacture recommendations. Therefore, the FDA should modify this statement to allow for manufacturers to use different cutoffs if their data supports it.

The use of benzodiazapines, barbiturates and tricyclic antidepressants as examples in the guidance is not appropriate, since this guidance does not address these types of assays.

Cut-off Validation Study Design

The use of a 25% above and below the cutoff is not appropriate for some the sample types and technologies that are currently available. For example, although the simple lateral flow membrane screening tests may not meet this precision standard; they perform well at 50% above and below the cutoff. These products provide reliable performance as a drug screening device. Additionally, for some types of samples, the cutoff levels are much lower than those used for urine drug testing. For example, an opiate urine test uses a cutoff of 2000 ng/ml, which at 25% above and below the cutoff, allows for a result between 1500 and 2500 ng/ml. However, when you are testing for much lower levels of drugs and cutoff levels, the same standard cannot be applied. For example, a saliva PCP that uses a cutoff of 10 ng/ml, using the same standard of 25% above and below the cutoff, would require that the test result fall between 7.5 ng/ml and 12.5

ng/ml. This is a standard that even many laboratories with lab-based products have difficulty meeting. FDA must take into consideration these variations as they continue to develop these guidelines. We recommend that FDA develop guidelines that have different requirement for:

Qualitative, semi-qualitative and quantitative assays – they should not be held to the same standard.
Level of detection. Assays with cutoffs at 1-20 ng/ml, 21 – 50 ng/ml, 51 – 100 ng/ml and greater then 100 ng/ml should have different precision requirements.

5. Method Comparison

These guidelines indicate that it is no longer necessary to compare your product to a predicate device if you compare it to GC/MS. This is not consistent with current FDA guidelines for 510(k) Prescription Use clearance. The ability to compare your product to a predicate device is the standard used to determine if a product can be submitted to the FDA using the 510(k) process rather than requiring a PMA.

The reference to barbiturates in this section is not appropriate, since barbiturates are not listed as being included in this guidance.

Study Design

The request for significant numbers of clinical sample at or near the cutoff is overly burdensome and onerous. It is not possible to determine in advance the levels of drugs in a sample. Additionally, clinical samples from street or recreational drug users, unlike prescription drugs users who will have a drug level in a narrow therapeutic range, have drug concentrations across the range of the assay. It would require a significant increase in the number of positive clinical samples in order to get a significant number at or near the cutoff. This is significantly more data than is currently required for a Prescription Use 510(k) for laboratory-based products.

We believe that it is inappropriate to legislate and pre-determine the sampling and distribution of the clinical study. The types of data that need to be collected will vary significantly depending on the type of specimen, the assay technology, the intended use of the product, the predicate device, and the manufacturers' claims for their product. We recommend that the structure of field evaluations be dictated by the sample matrix, assay sensitivity, accuracy and precision, as is currently done with most FDA cleared products. Consider that the LifePoint test system requires no user interpretive skills even around the cutoffs. This is not true for the visual membrane-based immunoassay systems. The clinical study sampling should certainly reflect this key difference. The sampling grid in the

guideline appears to single out the problems specifically associated with visual membrane-based systems.

The requirement to evaluate drug concentrations in samples over the range of possible results is appropriate; however, the example is not. With a focus on samples with drug concentrations between 50% below to 50% above the cutoff, there is no recognition of technology or sample matrix differences. Again, we point to low concentration cutoff levels; it is not realistic to request that for a cutoff level of 10 ng/ml that all the samples be tested between 5 ng/ml and 15 ng/ml. Additionally, there are some technology limitations. For example, lateral flow membrane technologies cannot meet this standard, and yet provide reliable screening results. We recommend that FDA provide guidance that takes into consideration these differences.

The use of tri-cyclic antidepressants in this section is not appropriate, since tri-cyclic antidepressants are not listed as being included in this guidance.

6. Stability

This is significantly more data than is currently required for a Prescription Use 510(k) for any product. This requirement would place onerous and overly burdensome requirements on manufacturers.

9. Studies in the Workplace and Other Sites Performing Repetitive Testing

The whole issue of user specific data generation and labeling is also very problematic as proposed. First, it is overly burdensome to require clinical data for each subset of professional use market. To require a manufacturer to try to perform expensive, difficult clinical trails in every single sub-market, is overly burdensome and onerous. This is especially true in some markets where the positivity rate is very low and it will take significant numbers of samples to obtain the needed number of positive results. The usual clinical trial design, using one representative site for professional use should be sufficient.

Additionally, the requirement to perform these studies in EACH environment that the product will be used is burdensome and onerous. It should be sufficient to provide data that shows that inexperienced users can use a specific product with reliable results, similar to the types of studies used for CLIA waver. But, within that context, it should be adequate to show: 1) a product gives results similar to a predicate device, and 2) a non-trained user will obtain results similar to a trained professional. The test system should provide both the non-trained user and the professional equal ability to obtain valid test results and should not require any correlation to a reference method (this is in the prescription part of the guidelines).

More importantly, the requirement to require workplace, school, sport, and insurance method comparison and precision studies, in addition to all of the data required by the previous eight (8) sections of this guidance, is overly onerous, burdensome and unfair. This requirement is significantly more stringent that those required for Prescription Use 510(k) for lab-based products

10. Home Use Consumer Studies

Study Design

We believe that it is inappropriate to legislate and pre-determine the sampling and distribution of the clinical study. The types of data that need to be collected will vary significantly depending on the type of specimen, the assay technology, the intended use of the product, the predicate device, and the manufacturers' claims for their product. We recommend that the structure of field evaluations be dictated by the sample matrix, assay sensitivity, accuracy and precision, as is currently done with most FDA cleared products. Consider that the LifePoint test system requires no user interpretive skills even around the cutoffs. This is not true for the visual membrane-based immunoassay systems. The clinical study sampling should certainly reflect this key difference. The sampling grid in the guideline appears to single out the problems specifically associated with visual membrane-based systems.

The requirement to evaluate drug concentrations in samples over the range of possible results is appropriate; however, the example is not. With a focus on samples with drug concentrations between 50% below to 50% above the cutoff, there is no recognition of technology or sample matrix differences. Again, we point to low concentration cutoff levels; it is not realistic to request that a cutoff level of 10 ng/ml be tested between 5 ng/ml and 15 ng/ml. Additionally, there are some technology limitations. For example, lateral flow membrane technologies cannot meet this standard, and yet provide reliable screening results. We recommend that FDA provide guidance that takes into consideration these differences.

The requirement to use pooled, spiked samples for the study design shows the bias toward lab-based urine products. It is simple to develop a series of negative urine sample pools and then spike them with the appropriate levels of drugs. This is not possible with other sample types, including sweat, hair and saliva. For example, a pool of saliva may change significantly even in a few hours. We recommend the FDA allow the use of either QC materials or standards that consist of liquid buffer with the targeted levels of drugs spiked into the sample.

IV. LABELING CONSIDERATIONS

A. GENERAL LABELING FOR DRUGS OF ABUSE SCREENING DEVICES

1. Intended Use

The requirement for a specific setting of use in labeling is onerous and burdensome. According to the proposed guidelines, a manufacturer will need to use user-specific labeling in each market. This becomes very problematic to implement when manufacturers, distributors, and even some service providers offer these products and services in multiple markets. It is overly burdensome and onerous to require the manufacture, distributor and users to manufacture, distribute and use a different product for each of these slightly different submarkets of the professional use category. As identified by FDA, these users have similar levels of training and skills and should not require such specific labeling to ensure proper use.

The suggested labeling identifying the minimum numbers of tests performed by an operator is inappropriate. Most of these products are very simple to use and even when used occasionally, will generate an accurate result. Some of the technologies and products are so operator-independent, it is almost irrelevant who performs the test. FDA needs to consider how the complexity of the products being used would change the oversight requirements in these environments. Since CLIA waived products assure an accurate result by a non-technical user, many of the proposed regulations are again inconsistent in the application of such products in a home or repetitive use environment.

The suggestion to indicate that any result, positive or negative, is only presumptive, is also not appropriate. If the result obtained using an on-site test is equal to or better than results generated by a lab-based method, then we also recommend that a confirmation test be required only when a confirmation would be required for the lab-based method. We recommend that a confirmation test be recommended on positive results only as is currently the practice in laboratory and professional use markets such as the workplace, schools, sports and insurance testing.

Additionally, the requirement that a confirmation test be done by GC/MS is not always appropriate. The use of a different method to confirm the initial result should be sufficient. This is current practice for many tests done either inside or outside of a laboratory environment. As an example, alcohol testing is normally done under DOT requirements and under state law for forensic use. In both situations, a second test is often considered a confirmation test. (This approach has been validated by the courts and is currently accepted by DOT and SAMHSA).

As a general comment, the proposed labeling guidelines are much more stringent than even the current requirements for a Prescription Use 510(k) product used in a laboratory by trained personnel. The proposed requirement that all of the proposed information in labeling for the professional repetitive use markets, such as the workplace, schools, sports and insurance and in some cases for the home use market, is unnecessary, and is likely to lead to more confusion by the user. A more focused presentation of the important information in a simple and easy to use format is much more likely to be understood. This is clearly a case of too much data confusing the important information. This is the type of information that should be requested in the submission, but not included in the labeling.

2. Summary and Explanation of the Test

There should be no obligation to restrict FDA clearance to products meeting SAMHSA cutoffs. SAMHSA only applies to the federally regulated workplace. Other regulatory bodies oversee the sports and insurance industries, and SAMHSA cutoffs may not be appropriate for those uses. FDA should not impose ANY cutoffs for results interpretation for drug of abuse testing. As with all other FDA cleared products, the recommended cutoffs for each product should be established and validated by the manufacturer of the product and then the final cutoff selected by the user, based on the use of the product. With drugs of abuse testing, the cutoffs selected will vary significantly depending on the use of the product (for example, there will be very different "cutoffs" for an overdose in the ER versus the testing for law enforcement, which is also often done in the ER). The SAMHSA guidelines may be appropriate for SAMHSA regulated markets only, and should not be automatically used by FDA.

The provision of pharmacokinetic data may not be appropriate or useful for screening assays, since most of the data found in the literature cites GC/MS results on samples obtained from single dose studies. We recommend that such data should not be included because the clearance rates are the result of multi-factorial influences, including level of drug dose, method of drug delivery, metabolic rate of subject and the sensitivity of the assay system used for drug detection. The inclusion of such data may be not only misleading, but, under some circumstances, incorrect.

3. Understanding the Test Result

The suggested wording in the proposed guidance shows a lab bias toward on-site test results. The examples used show a belief that these on-site products give marginal performance, which is not consistent with data generated even in FDA submissions for some of the products. For FDA to suggest this is standard performance is not appropriate.

Additionally, these data and the suggested wording for labeling are specific to on-site urine products only, and do not apply to other specimen types. We recommend that the labeling reflect the performance of the product being used and not general statements as suggested. Additionally, we recommend consideration be given to why a product might give a false positive or negative result such as the use of over-the-counter medications, etc.

The requirement for extensive labeling on false positive and false negative results is also not appropriate. Some drugs (cocaine, PCP or THC) rarely, if ever, give either laboratory false positives or positives from prescription medications. Therefore, if an on-site test is as accurate as a lab-based test, then a confirmation test should be performed only as desired by the user. We suggest the requirement for language that indicates that: "presumptive positive results for certain drugs (for example opiates and amphetamines) may be caused by prescription or OTC drugs and a confirmation test is strongly suggested".

Additionally, the mandatory confirmation requirement when applied to the professional use in the workplace, insurance, and sport, where there are procedures already established in the processing of a test specimen, is contradictory and not consistent with current practice. For example, the due process afforded employees by the requirement to have an MRO involved in the testing process is eliminated.

4. Quality Control

The requirement to evaluate QC materials with drug concentrations in the samples at 25% above and 25% below the cutoff is not appropriate, and shows no recognition of technology or sample matrix differences. Again, we point to low concentration cutoff levels; it is not realistic to request that for a cutoff level of 10 ng/ml that a 25% negative control is 7.5 ng/ml and a 25% positive control is 12.5 ng/ml. Additionally, there are some technology limitations. For example, lateral flow membrane technologies cannot meet this standard, and yet provide reliable screening results. More importantly, this proposed standard is significantly more stringent than the current QC practice recommended for Prescription Use products. Lastly, the ability of manufacturers to provide a QC material that will maintain such a tight level is not currently possible. Because of all these reasons, we strongly recommend FDA allow the use of current QC materials which are generally no drugs in the negative QC material, and 100% or more above the cutoff for the positive level.

5. Limitations

The requirement to specifically identify those markets that the product has not been labeled for, in the professional repetitive use markets, is onerous and burdensome. According to the proposed guidelines, a manufacturer will only be able to make claims in those markets in which extensive and duplicative

(therefore unnecessary) studies have been completed and data provided. As identified by FDA, these users have similar levels of training and skills and should not require such specific user specific clinical trials and labeling to ensure proper use. Therefore, we recommend that not only the labeling, but also the clinical trials, be for all repetitive use workplace type settings, such as sports, schools, and insurance testing.

Additionally, if user specific labeling is required, a different product with different labeling will be required in each market. (It will be very confusing to have multiple labeling of a single product even if it can be accomplished). This becomes very problematic to implement when manufacturers, distributors, and even some service providers offer these products and services in multiple markets. It is overly burdensome and onerous to require the manufacture, distributor and users to manufacture, distribute and use a different product for each of these slightly different submarkets of the professional use category.

6. Performance Characteristics

Cutoff Characterization and Analytical Sensitivity

The requirement to include all of the proposed data is not appropriate for all but the laboratory testing market. Even for that market, this requirement is much more stringent than currently required for labeling for a Prescription Use 510(k) product. To include operator specific data is onerous and unnecessary. This information should be included in the submission but not the labeling.

Comparison to predicate or reference methods

The requirement to include all of the proposed data is not appropriate for all but the laboratory testing market. Even for that market, this requirement is much more stringent than is currently required for labeling for a Prescription Use 510(k) product. To include the results at 50% below, near cutoff negative, near cutoff positive, 50% above the cutoff, is unnecessary and may be confusing to the operator. We recommend the current practice of a simple 4 X 4 grid that shows the positive and negative results as compared to the reference method.

General comment: The proposed guidelines indicate that the performance characteristics outlined may not be appropriate for home use tests. We strongly agree and also strongly recommend, in order to avoid confusion to the user, that the amount of information be limited in the labeling for the professional, repetitive use markets, such as the workplace, sports, insurance, etc.

B. SPECIAL CONSIDERATION FOR LABELING FOR HOME USE DEVICES

1. Overview

The statement "laboratory test is more accurate" may not be completely true and therefore, misleading. Some on-site test methods are actually more accurate than some methods that are used in a laboratory. We do not recommend the use of such wording.

The proposed example shows a bias toward lab-based urine tests. A confirmation test may not confirm the initial result, not because the initial result is incorrect, but because the second sample is probably collected at a different time. Timing issues are likely to play a larger role than incorrect testing when results are not confirmed. Rather than trying to explain where and how to get a confirmatory test, we recommend that a statement to consult with a healthcare professional be used rather than a mandatory confirmation test.

C. SPECIAL CONSIDERATIONS FOR LABELING OF WORKPLACE AND OTHER REPETITIVE SITE TESTING

The table identifies the proposed requirements for the labeling for each of the different market segments. With one exception, the proposed requirements for workplace or other professional use products are identical to laboratory use products. It is not appropriate to require the same type of information for products used by highly trained laboratory personnel as for repetitive market users, who do not generally have the same level of scientific education and technical training. We recommend the use of less data and more summary information that can be easily explained to the user. This is especially true for the labeling requirements outlined for performance characteristics, which should be simplified with the requirement that less important data be eliminated.

Additionally, according to the proposed guidelines, a manufacturer will need to use user-specific labeling in each market. This becomes very problematic to implement when manufacturers, distributors, and even some service providers provide these products and services in multiple markets. It is overly burdensome and onerous to require the manufacture, distributor and users to manufacture, distribute and use a different product for each of these slightly different submarkets of the professional use category. As identified by FDA, these users have similar levels of training and skills and should not require such specific labeling to ensure proper use.

D. OUTER BOX LABELING

1. For devices Intended for Laboratories and Workplace Settings

The proposed requirement to indicate that any result, positive or negative, is presumptive only, is also not appropriate. If the result obtained using an on-site test is equal to or better than results generated by a lab-based method, then we also recommend that a confirmation test be required only when a confirmation would be required for the lab-based method. We recommend that a confirmation test be recommended on positive results only as is currently the practice in laboratory and professional use markets, such as the workplace, schools, sports and insurance testing.

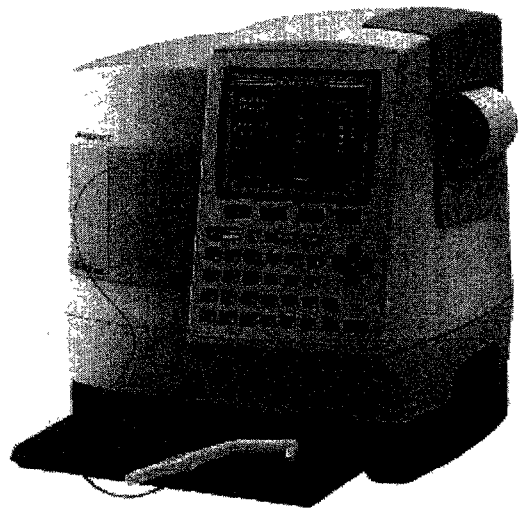
2. Labeling for Home Use Devices

A confirmation test may not confirm the initial result, not because the initial result is incorrect, but because the second sample is probably collected at a different time. Timing issues are likely to play a larger role than incorrect testing when results are not confirmed. Rather than trying to explain where and how to get a confirmatory test, we recommend that a statement to consult with a healthcare professional be used rather than a mandatory confirmation test.

Exhibit

LifePoint, Inc. is manufacturing and marketing the first non-invasive, on-site testing system that can deliver blood-comparable results without taking a blood sample. The LifePoint® IMPACT® Test System consists of an easy-to-use saliva collection and testing cassette, used in conjunction with a small, portable instrument. It is designed to be user friendly with minimal training required. The system is designed to quantitatively measure alcohol and screen for the five National Institute on Drug Abuse (NIDA) illicit drugs (marijuana, cocaine, opiates, methamphetamine/ amphetamine and angel dust (PCP) in a single cassette from a few drops of saliva within minutes. The system provides the following advantages:

- **Delivers under the influence results for drugs and alcohol**
- **Provides on-the-spot results**
- **Reduces chain-of-custody issues**
- **Minimizes training requirement**
- **Eliminates transportation issues**



The small, portable instrument automatically manages all functions related to running the test panel, including:

- **Specimen collection**
- **Sample adequacy and quality checks**
- **Automatic quality control**
- **Sample processing and analysis**
- **Electronic and hard copy test results**
- **Laboratory-quality accuracy and precision performance**
- **Result interpretation**
- **Legally defensible hardcopy results**

The test cassette, packaged in a foil pouch, is ready for immediate use and disposal. The saliva specimen, test reagents and waste are contained within the cassette, thereby greatly reducing the possibility of biological contamination.

The entire test procedure, including specimen collection and result printout, takes only a few minutes. Saliva is collected via aspiration, with a device similar to those used in a dental office, and automatically transferred into the test cassette. The average collection process itself takes less than one minute, which is significantly faster than absorbent pad collection (which can take five to fifteen minutes for sample collection alone). Additionally, aspiration allows for quantitative results, which cannot be provided with absorbent pad collection.

Saliva indicates blood-comparable or "under-the-influence" results, similar to a blood test. Saliva as a test specimen is therefore more relevant than urine for impairment related situations such as post-accident, for suspicion, random, and fit-for-duty tests or "current status' analysis such as for overdose testing in the emergency room. Urine as a test specimen indicates drug use over the last 2-5 days.

The IMPACT Test System is the first on-site system to test for drugs of abuse and alcohol simultaneously, and the first on-site test for blood-comparable "current status" or "under-the-influence" results. Additionally, the entire process – collection and test – is observable and significantly reduces the possibility of adulteration.